

aminers, in view of inaugurating and maintaining a vigorous campaign against violators of the law. The experience of a member of the Board shows the almost insurmountable obstacles encountered and the consequent need of the influence of the profession in prosecuting illegal practitioners, especially when, in the case of the licensed M. D., the most culpable of all offenders, the friends of the defendant, the faculty of his alma mater, flock to the judge's chambers or to the witness-stand to give the defendant a good character. The illegal practitioner expects to find, and does find, protection and immunity in the medical profession itself, which so often gazes silent, indifferent and apathetic upon some enthusiasts who, single-handed, are doing the dirty work in the lower courts of justice.

For the sake of principle the conviction of one educated violator of the law would do more good than the imprisonment of ten ignorant fakirs. Fellow members, I again urge that the directors of this Society devise some plan of co-operation between the County Societies and the Board of Examiners.

I thank you for your attention and your support, to which we must attribute whatever good we may have accomplished. The endorsement of our work by official and educational circles of other States is but the echo of your generous support.

SPECIFIC THERAPY IN TUBERCULOSIS.

By GEORGE H EVANS, M. D., San Francisco.

Nearly 17 years have elapsed since Koch made the remarkable announcement of the discovery of a remedy prepared from a concentrated culture of the tubercle bacillus for the treatment of tuberculosis. The events of the year or two following this announcement are vividly impressed in the memory of all of us who were interested in this great subject at that time, and Koch's laboratory became the Mecca of hundreds of students in tuberculosis from every land, who hurried thither, filled with the hope that the great savant, whose name was so intimately linked with the scientific progress of discovery and achievement in this malady, had really solved the problem of specific medication. We know, likewise, only too keenly, the bitter disappointment of those who, on returning to their homes, applied tuberculin, a remedy prematurely announced by its discoverer, insufficiently understood, unintelligently applied in improperly selected cases, with results which, under such conditions of administration, were inevitable. The hope of the discoverer and his followers was not realized, and tuberculin, as far as the general profession was concerned, sank for the time being into disrepute and oblivion. In the years which have intervened, however, the fundamental facts on which tuberculin therapy depends have been undergoing elaboration, and, with our ever increasing knowledge of the laws of immunity, our conception of the role which tuberculin plays has undergone great modification, and, as far back as 1897, when Koch produced his new tuberculin T R, which consists of the entire substance of the tubercle bacilli, the old conception that tuberculin had direct curative action had been abandoned. It is with the abandonment of this old conception, and the development of tuberculin as a vaccine, and by

a vaccine I mean a "substance which, when introduced into the body, causes there an elaboration of protective substances," that the present day conception of tuberculin therapy has arisen.

The way has been long and intricate that has been traversed by the investigators of the laws of immunity, and the clash of the arms of the opposing schools has resounded time and again throughout the scientific world. The theories of Ehrlich and Metchnikoff are, however, in accord, in essential results; and if one accepts Metchnikoff's definition of immunity against infective diseases as "the group of phenomena in virtue of which an organism is able to resist the attack of micro-organisms that produce these diseases," the question whether the leucocyte must be regarded as the source of the bactericidal substance of the body fluids need not particularly concern us in this discussion; for both schools have a common point in the admission of a cellular immunizing property.

The fact of the artificial induction of immunity is accepted to-day as a fundamental principle in medicine as the result of the labors of Jenner, Pasteur, Behring, Wright, and others; but the brilliant achievements of the latter investigator have opened up new fields in therapy hitherto impossible of attainment. While Ehrlich, Buchner, Pfeiffer, and others, had shown the protective properties of immune sera, it remained for Wright to demonstrate practically the presence of bacteriotropic substances (opsonins) in the blood serum, and, by a most ingenious technic, to determine the quantity of this substance, and to show conclusively the effect of the inoculation of vaccines on its content. The nature of these opsonic bodies is of great interest. They unquestionably must be classified along with other bacteriotropic bodies, which are known to exist: e. g., antitoxins, agglutinins, precipitins, and lysins. This theory can be very well reconciled with the fundamental principles of the schools of Metchnikoff and Ehrlich, and they would appear to have a similar function to fixatives or amboceptors, in that they either have a chemical affinity for both bacteria and cytases, or they sensitize the elements to the fermentative action of the cytases.

The practical application of this discovery to tuberculin therapy is not far to seek, and the events which follow the inoculation of tuberculin can be best given in Wright's own words, which I quote from a communication to the Royal Medical and Chirurgical Society:

"Upon the inoculation of the vaccine there supervenes a period of intoxication which is characterized by a decline in the anti-bacterial power of the blood. This 'negative phase' is more or less accentuated and prolonged according as a larger or smaller dose of the vaccine is inoculated. In the former case the 'negative phase' may disclose itself to clinical observation by a temperature reaction and constitutional disturbance. In the latter case the 'negative phase' may be quite unaccompanied by clinical symptoms. Upon the 'negative phase' there follows a 'positive phase.' This phase, whose characteristic

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feature is an increase in the antibacterial power of the blood, corresponds to a period of increased resistance. The curve whose trace sets forth the changes in the antibacterial power of the blood, runs up in many cases into a sharp peak and sinks away first comparatively rapidly and afterwards more slowly. There is associated in many cases with the climax of the 'positive phase' a sense of increased physical vigor and a very pronounced feeling of well-being. After the negative and positive phase, which train of events I have ventured to speak of as the 'ebb and flow and reflow of the tide of immunity,' the blood may be maintained for a variable period at a somewhat higher level of antibacterial power than before inoculation. Or, the antibacterial power of the blood may over and over again fall back after ten days or a fortnight to the level at which it stood anterior to inoculation."

By means of successive inoculations of tuberculin, at intervals governed by the opsonic index of the patient, which is arrived at by the comparative content of opsonins, with that of serum from a normal individual, the amount of these bacteriotropic substances is continuously increased until it is considerably in excess of that of the normal person. I do not wish to enter in detail into a consideration of the technic of opsonic observations, for the literature has been replete with it during the past year, but this paper would be very incomplete if the question of its practical applicability were not freely discussed. I do not believe that any one who has had the privilege of visiting Wright's laboratory and seeing the work there, can fail to be convinced of the accuracy of his methods, nor can the statement be gainsaid that we have in this method an accurate way of determining the amount and interval of tuberculin dosage. I do not believe, however, that Wright's method can be of universal application in clinical work in private practice until the elaborate technic necessary has been very much simplified, and as Bulloch, who is probably Wright's most enthusiastic disciple, has well said, the performance of the procedures advocated by Wright requiring time, skill, and the use of a laboratory, the problem will perhaps best be solved by our great hospitals undertaking, to a large extent, work of this class. An element of danger also exists in the fact that inaccurate results will necessarily be recorded unless the work is entrusted to skillful laboratory workers—results that will be fraught with serious consequences; for that the possibility of error is great, no one who has had any practical experience with the opsonic technic will deny. These facts place a limitation on the practical value of Wright's findings as a guide to therapy.

Again, considerable confusion exists regarding the classification of several bacteriotropic substances, found in the blood, and the relationship of opsonins to some of the other anti-bacterial bodies has not been sufficiently determined. It is reasonable to suppose, and indeed it can be demonstrated, that injections of tuberculin cause an increase of agglutinins as well as opsonins, and at the present time I am engaged in experimental work with the purpose of

utilizing the agglutinins as a guide to tuberculin dosage, by a technic more simple, and therefore with less element of error, than the more elaborate technic of Wright.

Uhl has been applying Arneth's methods of classification of the neutrophile leucocytes, as a means of tracing the progress of tuberculous processes under tuberculin treatment, at the Edmundsthal Sanatorium in Germany, with satisfactory results. Arneth, in a recent exhaustive monograph, has described his studies of neutrophiles in infectious diseases including tuberculosis, and gives a resume of his investigations in the latter disease. He adopts a classification of neutrophiles dependent on the number of nuclei, the cells with the more complex nuclei being considered the riper and more efficient ones. By an adaptation of this classification he has been able to demonstrate the relation between the course of the disease and the blood picture, and in this way applies the latter as an index of the defensive and protective efforts of the body against the infection. This work has been elaborated by Klebs of Chicago, who made a very thorough report at the last meeting of the National Association for the Study and Prevention of Tuberculosis.

Whatever the ultimate outcome of Wright's technic may be, however, as a guide for the administration of vaccine, his researches and magnificent achievements have done much to remove tuberculin therapy from the realm of empiricism, and have absolutely demonstrated its definite scientific value in treatment. In doing this he has demonstrated the fact that the greatest yield of protective substances is not produced by dosage sufficient to cause constitutional disturbance, and that the capacity of the organism for immunizing response is limited. In this light the failure of large doses of tuberculin is made apparent, and any dose sufficient to cause febrile reaction can only be looked upon as injurious.

As has been said above, it is with the recognition of the fact that the body must become immune to the entire bacillus and its products, that the present day conception of specific therapy had its inception. Buchner has clearly shown that some of the immunizing property seems to be in the albuminates of the bacterial cell. The specific poisonous substances found outside the parasites in the culture fluids are not identical with the protective substance occurring in the disease germs, or their metabolic products. Admitting this, we must necessarily turn from the products of bacterial cultures, such as old tuberculin, and look to those products which contain the endogenous toxins of the bacillus, for immunizing and curative properties. The studies of Koch, Behring and Pearson in bovine immunity produced by the injection of living human bacilli, and the same experiments by Trudeau on smaller animals, bring us back to the old principle first brought out by Pasteur in 1880 in his studies of protective inoculation toward fowl cholera. Theobald Smith and others, however, have shown the immunizing value of injections of killed bacilli; and it is significant that Behring, in his announcement before the Paris

Congress, stated that his experience had led him to a definite determination to abstain from introducing into the human body, for any therapeutic purpose, living tubercle bacilli.

At present it is unknown which substances of the bacillus plays the most important and decisive role in arousing the defensive reaction of the body, and hence the necessity of using such product as contains them all. Of the different preparations, my own experience during the past four years has been principally with Koch's T R, and von Ruck's watery extract of tubercle bacilli. The former consists of an extract of the ground unheated bodies of tubercle bacilli; the latter consists of the pure tubercle proteids dissolved out of the bacillary pulp by sterile distilled water after the fats have been extracted by sulphuric ether.

No more auspicious occasion could have been chosen than that of the meeting of the International Congress at Paris in 1905, when the eyes of the medical profession were steadfastly turned to that notable gathering, for the announcement to come from Behring, of the discovery of the existence of a curative principle depending for its activity upon the impregnation of the living cells of the organism by a substance proceeding from the virus of tuberculosis, and which he designated T C. When the T C has become an integral part of the cells of the organism, and has been metamorphosed by these cells, he designates it by the formula T X. In order to free the T C from substances which hinder its therapeutic action, he distinguishes three groups of bacillary substances, which he removes from the bacillus. It is then, from the remaining body, or "restbacillus," which it is claimed still retains the form and staining qualities of the tubercle bacillus, that the specific body T C. is obtained. No therapeutic results have as yet been reported from the use of this preparation.

Maragliano, who has been working for several years on the possibility of producing passive immunization by means of the milk of immunized cows, has succeeded, by means of inoculations of the filtrate of living and virulent tubercle bacillus cultures and bacillary pulp, into cattle, in producing a serum which protects experimental animals against the poisons of the tubercle bacillus, and also against the tubercle bacillus itself in pure culture, when given in doses which do not overwhelm the animal, but which have been shown to be fatal. The curative value, however, has not been sufficiently established, and results reported from the Phipps Institute from its use have not been promising.

Marmorek, then connected with the Pasteur Institute, in 1903 produced a serum for vaccination and treatment, based on the theory that tuberculin was not the specific toxin of the tubercle bacillus; hence it was impossible for it to elaborate specific antibodies for that bacillus. Marmorek's serum is prepared by injecting horses with cultures grown on such culture media as, in the opinion of the inventor, produced the specific toxin, almost to the

exclusion of tuberculin. While good results have been claimed by some, the serum has been severely condemned by French investigators. Prof. Hoffa of Berlin has, however, been very recently getting good results from its use in bone and joint tuberculosis, having reported forty such cases, the majority of which have been most beneficially influenced by the use of Marmorek's serum.

Dr. Baldwin has truly said that "ignorant haste, both in its use and condemnation, characterizes the history of tuberculin treatment," and this is particularly true as regards the selection of patients suitable for treatment. I believe it should be an axiom that tuberculin has no place in the treatment of acute cases of tuberculosis, for in such the machinery of immunization is paralyzed, by continuous auto-inoculations of toxins from the foci of infection. In all pyrexial cases it should be our aim to bring the infection to a condition of a purely localized infection by rest in bed and other appropriate methods. When this has been accomplished, we should endeavor to substitute for the inappropriately adjusted, and inappropriately interspaced auto-inoculations which wore down the patient without achieving effective immunization, a system of appropriately adjusted and appropriately interspaced inoculations of a tubercle vaccine. The greatest benefit from tuberculin treatment will be found in early cases, and in those chronic cases which, with a fair amount of disease, and a fair amount of cirrhosis and healing, are however stationary.

It will be urged by the opponents of tuberculin therapy, that this remedy possesses no advantages over the hygienic, open-air methods whereby natural immunizing results are acquired; that the curability of tuberculosis by nature's methods is daily demonstrated on the autopsy table on subjects who have died from other causes; that the magnificent results obtained in Sanatoria by prolonged open-air methods attest more eloquently than arguments of speech, the efficacy of such treatment. Our knowledge of the pathology of tuberculous lesions, and of the nature of the tubercle bacillus, must convince us that the chronicity of this disease is due to the difficulty with which specific toxins are liberated. The latency of tubercle in the tissues is, I believe, frequently the condition that is mistaken for cure in those discharged from Sanatoria; for large numbers of "cured" Sanatorium patients, where hygienic measures were alone carried out, have been known to have low opsonic indices. The cure of bacterial infections, tuberculous or otherwise, is not directly dependent on the breathing of fresh air, whether obtained in the arid regions of Arizona, in the balmy climate of Southern California, or in tent life at home; nor upon the deposition of fat in the tissues from forced feeding and prolonged rest. All these measures, valuable though they are, will fail, if the destruction of the invading bacteria is not accomplished, through the elaboration of the anti-bacterial substances in the blood.

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EARTHQUAKE SHOCK CONSIDERED AS AN ETIOLOGICAL FACTOR IN THE PRODUCTION OF MENTAL AND NERVOUS DISEASES.*

By JOHN W. ROBERTSON, M. D., Livermore.

The earthquake of April, 1906, and the social and individual disturbances based upon it are so far reaching, so many phased and, in some instances so badly distorted, that even the year which has elapsed cannot give us a full understanding of the real neurotic disturbances which can be properly charged to it.

It cannot be doubted that there was an absolute mental effect produced on the great majority of those who experienced this shock; and that this was intensified by the terror of the subsequent conflagration on those who were compelled to participate in the refugee environment; but just what part is to be attributed to the fright and what to the personal loss and the changed condition of social life is difficult of analysis.

It seems certain that, immediately following the earthquake and properly to be attributed to it was a condition of nervous shock—of a mental state bordering on stupor; possibly best described as a depressive condition having, as a pathological basis, a change of cerebral circulation. Apparently this varied in direct proportion to the nervous temperament but even the most coolheaded were slightly obsessed. There soon followed a condition of well-being, of thankfulness that they still lived—mild excitement not so much shown by hysteria as by exaltation—a condition possibly of slight cerebral congestion. Many stories illustrative of this phase were told and seemed to be a part of every day observation of those who lived with and were a part of the San Francisco population. Some of these acts showed such complete mental unbalance as not to be compatible with sanity. Many have remarked on the curative effect of the earthquake; of paralytics who walked, chronic invalids suddenly regaining normal health and even those who had long believed that they suffered from heart disease suddenly resuming their old active life. In

other words the earthquake was to many invalids a command, "Take up thy bed and walk," and while the cerebral congestion remained, immense energy was displayed and suggestive cures were possible.

The mental attitude of the whole population was reported to be one of exaltation. Though the first day had shown the immensity of the catastrophe and the three days' fire added to its terror, there were but few reports of breakdowns, of mental depression, or any real consciousness or appreciation of the great danger which certainly did exist and was patent to all. In spite of the calamity very many treated it as a huge joke, were hilarious and, if they felt disturbed, gave no outward sign. These acts were often regarded merely as an evidence of buoyancy, hopefulness and untamable spirit of the San Franciscan—not as a pathological brain strain.

Many assertions have been made regarding the causative influences of the earthquake and its attendant ills on the production of insanity. It must be remembered that mental alienation cannot be produced at will, that the normal brain does not easily give way to stress and that, in all cases, we suppose as a basis of insanity not only a nervous diathesis but a predisposition to that form of nervous instability which has for a basis disturbed cerebral circulation. This fact is overlooked by many committing physicians, and our asylum records are rendered worthless, etiologically speaking, because of this misconception. If the brain, by inheritance, be unstable, any disease of any organ may cause mental unbalance. We practically ignore the emotions as predisposing factors, though it may be true that, in a brain weakened, these may act so profoundly as to either hasten or actually precipitate insanity. As a rule disturbance of the emotions is merely the first symptom.

Beyond question, in certain patients already mentally weakened, active brain disease was induced by the fright, worry and discomforts experienced during the earthquake disturbance; yet the vast number for which this is assigned as a cause has no basis in fact.

Study of the records does not bear out the fact of increase. Taking the statistics as furnished by individual asylums, that of Southern California has been ignored as not being in the earthquake zone, nor can Agnews be considered because of its total destruction.

Dr. Stone, Superintendent of the State Hospital at Napa, reports 266 patients admitted during the year 1905; while for the year 1900 there were 334—an increase of 68 for the earthquake year.

Dr. King of Mendocino also reports an increase of 42, there having been 236 admissions in 1906 and only 196 for the preceeding year.

Dr. Clarke reports an increase of only 10—432 against 422. This increase could be easily accounted for by the greater number of patients necessarily sent to the other three asylums because of the destruction of Agnews. Yet we find that of the 120 increased admissions, 69, or 60 per cent,

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